

FIG. 1

N-Z				
#	STRUCTURE	Ki(M) ^a	R ^b	METHOD
3)	0.080	20	
4	2-Z 2-Z 2-Z 2-Z 2-Z 2-Z 2-Z	0.010	400	IX, XIII
5		0.010	210	XIII
6		0.005	220	XIII
7		0.10	3.6	III
8		0.110	3.7	II
9	" " " " " " " " " " " " " " " " " " "	0.440	2.7	IV
10	Z-Z Z-Z Z-Z Z-Z Z-Z Z-Z Z-Z Z-Z	0.050	>10	XV
11	2-z 	0.190	2.4	XV

a INHIBITION OF POLYAMINE UPTAKE: KI DETERMINED FROM LINEWEAVER-BURKE **DOUBLE RECIPROCAL PLOTS**

FIG. 2

b INHIBITION OF TUMOR CELL GROWTH: R IS RATIO OF IC50 (COMPOUND ALONE) TO IC50 (COMPOUND + DFMO)

c NUMBERS REFER TO EXAMPLES (DESCRIBING SYNTHESIS)
d PURCHASED FROM ALDRICH CHEMICAL COMPANY



#	STRUCTURE	Ki(M) ^a	R ^b	METHOD
12		0.150	4.3	XV
13		0.058	>47	XV
14	z-z-z-	0.037	14	XVII
15	Z-Z	0.091	2.2	II
16		0.08	2.1	XV
17		0.43	>31	XV
18		0.083	40	XVII
19		0.24	>10	XV
20		0.28	1.0	XVII
21		0.084	1.0	XVII

FIG. 2 (CONT.1)



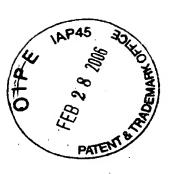
#	STRUCTURE	Ki(M) ^a	R⁵	METHOD
22		0.066	. 11	XV
23		0.250	6.2	ll .
24	H 2-1	0.23	10	XV
25		0.067	8.6	XV
26		0.180	15	XV
27		0.650	9.9	XV
28		0.054	9.3	XV
29		0.076	>46	XV
30		0.120	>10	XV
31		0.083	>12	XII

FIG. 2 (CONT.2)



#	STRUCTURE	Ki(M) ^a	R ^{b.}	METHOD ^c
32		0.093	2.1	XVII
33	T - Z - T - Z - T - Z - T - Z - T - Z - T - Z - T - Z - T - Z - Z	0.17	1.4	XV
34	H 2 H 2 H 2 H 2 H 2 H 2 H 2 H 2 H 2 H 2	0.120	1.0	XV
35		0.041	33	XIII
36	H N N N N N N N N N N N N N N N N N N N	0.61	>2	XVII
37	H N N N N N N N N N N N N N N N N N N N	0.150	2.4	XVII
38		0.140	1.0	XVII
39		0.500	1	XVII
40		0.086	18	XVII
41		0.200	1.0	XVII

FIG. 2 (CONT.3)



#	* STRUCTURE	Ki(M) ^a	R⁵	METHOD ^c
42		0.110	1.1	XIV
43		0.033	76	XVII
44		0.073	39	XIII
45		0.052	3.0	XIII
46	2-z 	0.082	63	XIII
47	2 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	2.1	6.8	XII
48		0.079	>49	XII
49		0.067	3.2	XV
50		0.12	1.0	XVII
51		0.083	1.5	XV
		<u>. </u>		_!

FIG. 2 (CONT.4)



#	STRUCTURE	Ki(M) ^a	R ^b	METHOD°
52		0.094	5.3	XV
53	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.18	1.0	XV
54	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.19	2.0	XV.
55		0.079	>1.1	IV
56		0.190		d
57		0.017	170	XV
58		0.050	189	XIII
59			>1	XIII
60			>1	XIII
61	*	0.200	1.0	XIII

FIG. 2 (CONT.5)



#	STRUCTURE	Ki(M) ^a	R ^b	METHOD°
62	"		>2.0	XIII
63		0.050	>1	XIII
64	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.046		XIII
65		0.012	·	XIII
66		0.018	27	XIII
67		0.07	1.0	XIII
68		0.110	>4.4	XIII
69	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.22	1	XV
70		0.033	>12.2	XIII
71		0.160	>1.5	XIII

FIG. 2 (CONT.6)

/	AP45 3	Sitte
d	19	<u>ي</u> ر
0	FB 2'8	DEMAR
	PATENT	S. C. S. C.

#	STRUCTURÉ	Ki(M) ^a	R⁵	METHOD ^c
72		0.031	>100	XIII
73	→°, H,	0.094	>1	XIII
74		0.200	1.0	XIII
75		0.130	>1	XIII
76		0.040	1.0	XIII
77		0.093	1	XIII
78		0.156		XIII
79	H N H N H N H N H N H N H N H N H N H N	0.047	1	XIII
80	H-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N	0.258		XIII
81		0.0096	153	XIII

FIG. 2 (CONT.7)



#	STRUCTURE	Ki(M)a	R ^b	METHOD ^c
82		0.097	>54	XIII
83	H-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N	0.183		XIII
84	H-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N	0.036	>3.2	XIII
85		0.048	>6.5	XIII
86	H-7-1- N-1- N-1- N-1- N-1- N-1- N-1- N-1-	0.091		XIII
87		0.034	>1	XIII
88		0.014	>40	XIII
89		0.020	>1	XIII
90		0.077		XIII
91		0.037	1	XIII

FIG. 2 (CONT.8)

#	STRUCTURE	Ki(M) ^a	R⁵	METHOD ^c
92		0.300	1	XIII
93	→ °	0.061	1	XIII
94		0.042	1	XIII
95	H_Z_T_T_Z_T_T	0.050	1	XIII
96		0.034	1	XIII
97		0.027	1	XIII
98		0.180	12	d

FIG. 2 (CONT.9)



SULFONAMIDES

102

WHERE

X=HALIDE OR N-HYDROXYSUCCINIMIDE ESTER R=HEAD GROUP POLYAMINE=SPERMINE (OR OTHER) Y=O OR S OR NHR

(CORRESPONDING TO UREAS, THIOUREAS AND GUANIDINES, RESPECTIVELY)



FIG. 5



FIG. 7

FIG. 8

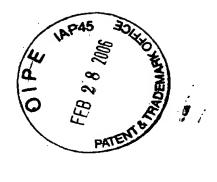


FIG. 9



$$H_2N \longrightarrow N \longleftrightarrow_X NH_2$$
 $111a$
 $112a$
 $H_2N \longrightarrow N \longleftrightarrow_X NH_2$
 $111b$
 $112b$
 $H_2N \longrightarrow N \longleftrightarrow_X NH_2$
 $111b$
 $H_1N \longleftrightarrow_X NH_2$
 $H_2N \longleftrightarrow_X NH_2$
 $H_1N \longleftrightarrow_X NH_2$
 $H_2N \longleftrightarrow_X NH_2$
 $H_1N \longleftrightarrow_X NH_2$
 $H_2N \longleftrightarrow_X NH_2$
 $H_2N \longleftrightarrow_X NH_2$
 $H_1N \longleftrightarrow_X NH_2$
 $H_2N \longleftrightarrow_X NH_2$
 $H_1N \longleftrightarrow_X NH_2$
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 $H_2N \longleftrightarrow_X NH_2$
 $H_1N \longleftrightarrow_X NH_2$
 $H_1N \longleftrightarrow_X NH_2$
 $H_1N \longleftrightarrow_X NH_2$
 $H_2N \longleftrightarrow_X NH_2$
 $H_1N \longleftrightarrow_X NH_2$

FIG. 10



$$H_2N$$
 H_2N
 H_2N

$$H_2N$$
 H_2N
 H_2N
 H_2N
 H_3N
 H_4N
 H_4N

COMPOUND 1391 L-LYS-SPM(METHYLAMIDE)

$$\begin{array}{c|c} H_2N \\ & \downarrow \\ CH_3H \\ & \downarrow \\ N \\ & \downarrow \\$$

$$H_2N$$

$$X = 1 \text{ TO } 3$$

$$Y = 0 \text{ TO } 3$$

$$H_2N$$

$$X = 1 \text{ TO } 3$$

$$Y = 0 \text{ TO } 3$$

$$H_2N$$

$$X = 1 \text{ TO } 3$$

$$Y = 0 \text{ TO } 3$$

COMPOUND 1393-1405 L-LYS-SPM(ISOAMIDE)

COMPOUND 1202 AND VARIATIONS THEREOF.

FIG. 11a

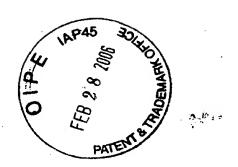


PATERY & PAT

LAH, THF

 $R=-COCH_3$, 47 $R=-CH_2CH_3$, 77

FIG. 11b



CROTONIC PUTRESCINE DCC, THF

119

15%

$$A_{3}$$
 $A_{43\%}$

PUTRESCINE DCC, THF

119

 A_{118}
 A_{118}
 A_{119}
 A_{118}
 A_{119}
 A_{118}
 A_{119}
 A_{118}
 A_{119}
 A_{119}



OTHER ANALOGS:

126a



$$CO_2H$$
 H_2N
 NH_2

D OR L-ORNITHINE

$$H_2N \longrightarrow N \longrightarrow NH_2$$

$$132$$

$$H_2N \longrightarrow N \longrightarrow NH_2$$

$$H_2N \longrightarrow N \longrightarrow NH_2$$

$$H_3N \longrightarrow N \longrightarrow NH_2$$

$$H_3N \longrightarrow N \longrightarrow NH_2$$

$$H_3N \longrightarrow N \longrightarrow NH_2$$

WHERE

Y=O, S OR NH;

R= VARIOUS GROUPS INCLUDING: PROPYLAZIRIDINE, PROPYLAMINE

HEXYLDANSYLSULFONAMIDE

R₁= H, CH₃(CH₂)_n-,WHERE n=1 TO 10; X= H OR HALOGEN



$$X_{R_1}$$
 X_{R_1}
 Y_{R_2}
 Y_{R_2}
 Y_{R_1}
 Y_{R_2}
 Y_{R_2}
 Y_{R_1}
 Y_{R_2}
 Y_{R_2}
 Y_{R_1}
 Y_{R_2}
 Y_{R_2}
 Y_{R_1}
 Y_{R_2}
 Y_{R_1}
 Y_{R_2}
 Y_{R

137

WHERE X= SPACER₁, Y= SPACER₂; AND Z= SPACER₃; AND R₁, R₂ AND R₃ CAN BE ALICYCLIC, AROMATIC, OR HETEROCYLIC

FIG. 15

-C2 "HEADLESS" -C3 "HEADLESS" -C6 "HEADLESS" -NO DFMO EFFECT OF "HEADLESS" COMPOUNDS ON THE GROWTH OF MDA-MB-231 CELLS WITH ODC INHIBITORS 300 100 30 9 RELATIVE CELL 60% - GROWTH 100% 80% - %0 20%. 120%. 40%

FIG. 17

[HEADLESS] µM



⊢C2 "HEADLESS" ►C3 "HEADLESS" -C6 "HEADLESS" -NO DFMO EFFECT OF "HEADLESS" COMPOUNDS ON THE GROWTH OF PC3 CELLS WITH ODC INHIBITORS 300 100 30 9 0.4 0.8 0.6 0.2 RELATIVE GROWTH



FIG. 18

[HEADLESS] µM



STEREOCHEMISTRY: L IS S, D IS R

<u>R'</u>		<u>R'</u>	
-Н	Gly	HS ~	Cys
-CH ₃	Ala	`s~~	Met
>	Val	H₂N → O	Asn
	Leu	H_2N \bigcap O	Gln
	lle	HO Y	Asp
	Phe	но т	Glu
но	Tyr	H_2N	Lys
	Trp	H ₂ N	Orn
HO V		$H_2N \underset{NH}{\overset{H}{}} N \underset{NH}{}$	Arg
ОН	Ser	V √ √ √ √ √ √ √ √ √ √ √ √ √ √ √ √ √ √ √	His
		N H O OH	Pro



FIG. 20

$$H_2N$$
 H_2N
 NH_2
 NH_2

FIG. 21

DACS WITH ODC INHIBITOR ENHANCES THE GROWTH-INHIBITION OF MDA-MB-231 BREAST CARCINOMA CELLS

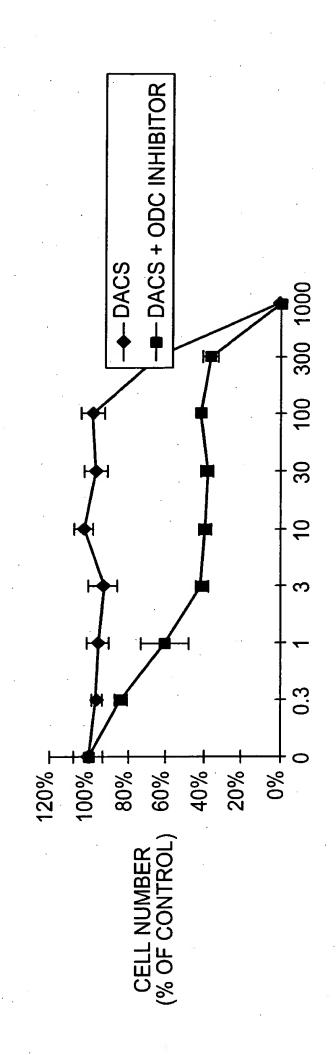


FIG. 22

[DACS] (µM)





DACS INHIBITS GROWTH IN THE PRESENCE OF 1.0 μM SPERMIDINE

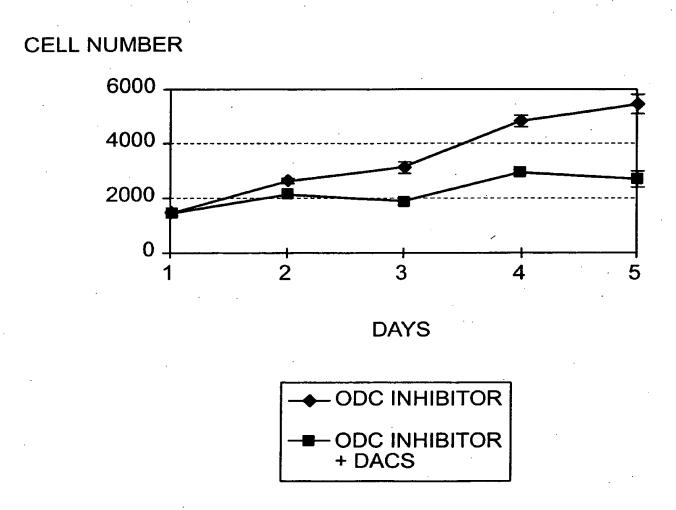


FIG. 23

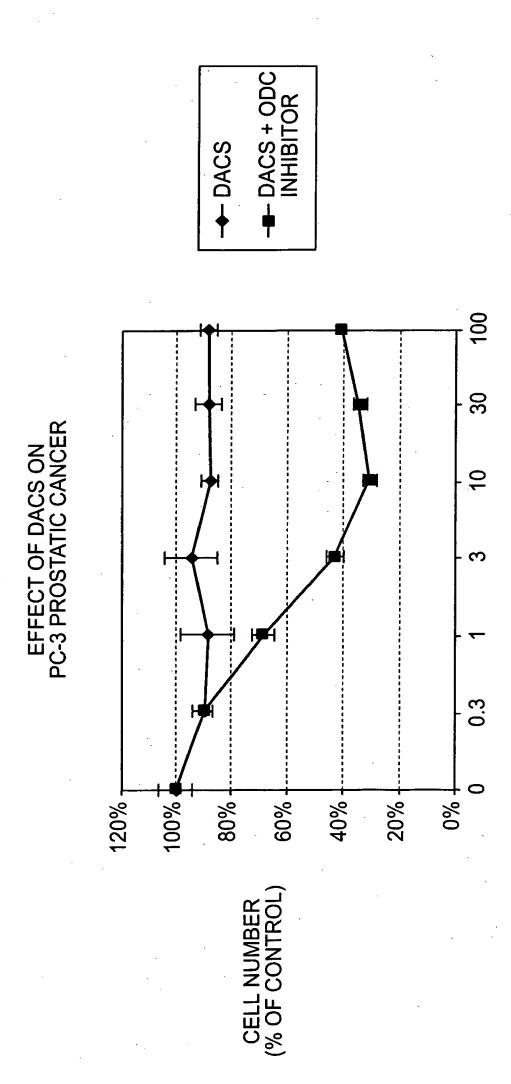


FIG. 24

[DACS] µM





$$\begin{array}{c|c}
H_2N \\
\\
N \\
\\
\hline
 & 161
\end{array}$$

TRIFLUOPERAZINE

IMIPRAMINE

THORAZINE

$$\begin{array}{c|c}
 & \circ \\
 & \circ \\
 & \bullet \\$$



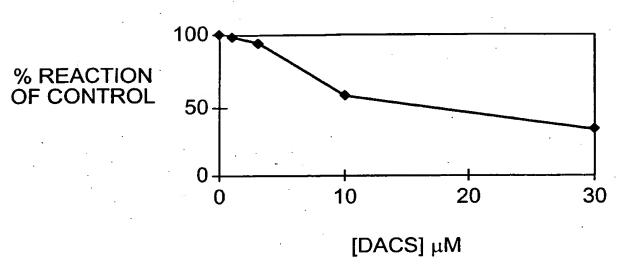


FIG. 26



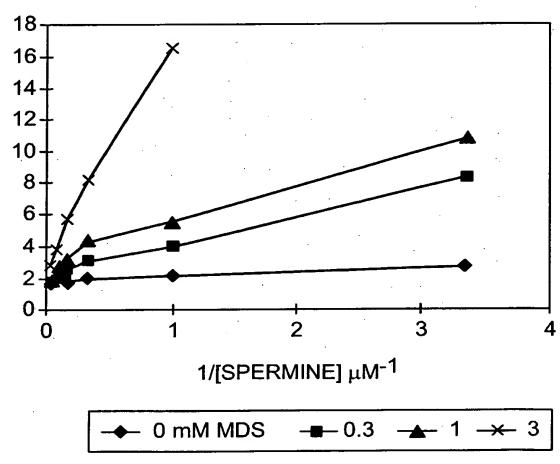


FIG. 27

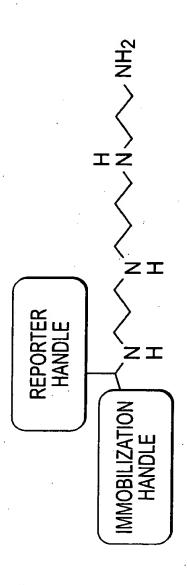
1000 ■—A172 W/2 mM DFMO 48 HOUR INCUBATION 800 600 [MDS] (µM) 400 200 -A172 10-9 PMOLE MDS/ MIN/MILLION CELLS

FIG. 28

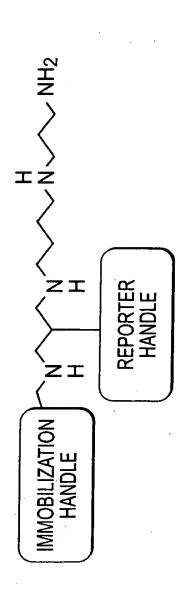


FIG. 30

A. REPORTER AND IMMOBILIZATION HANDLES ARE BOTH N1-TERMINAL



B. REPORTER HANDLE IS INTERNAL AND IMMOBILIZATION HANDLE IS N-TERMINAL



C. IMMOBILIZATION AND REPORTER HANDLES ARE BOTH N1- N12 TERMINAL, RESPECTIVELY





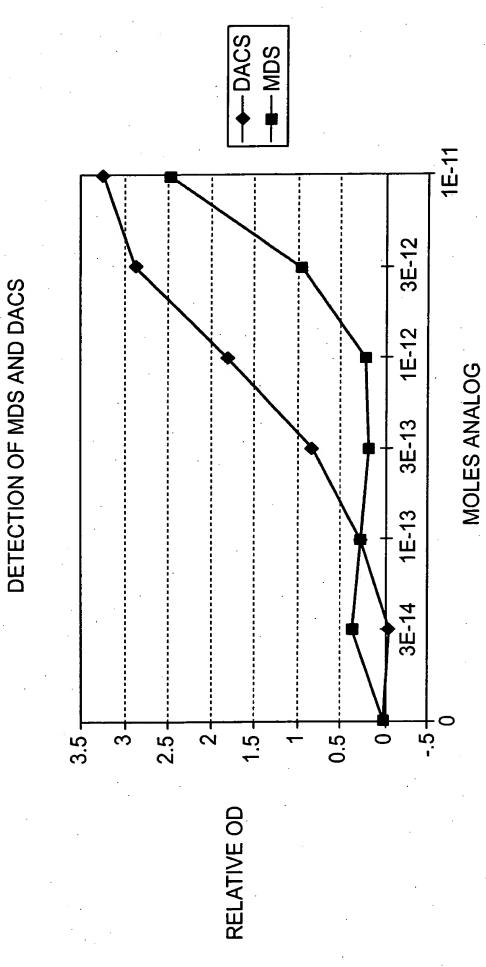


FIG. 32

GENERAL SCHEME

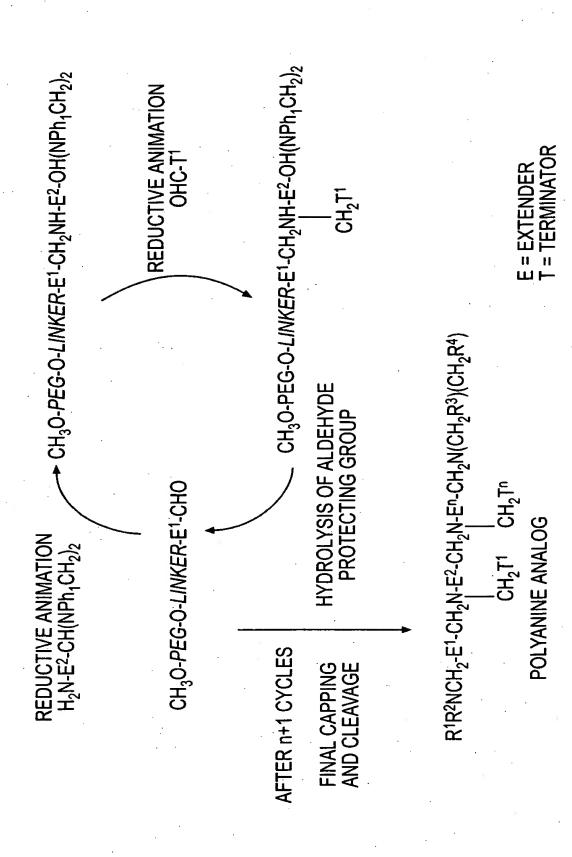


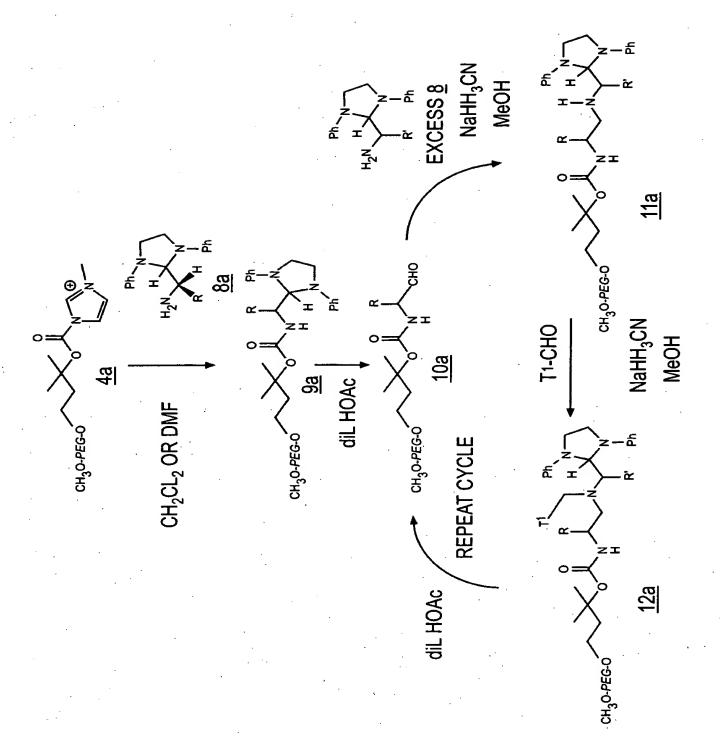




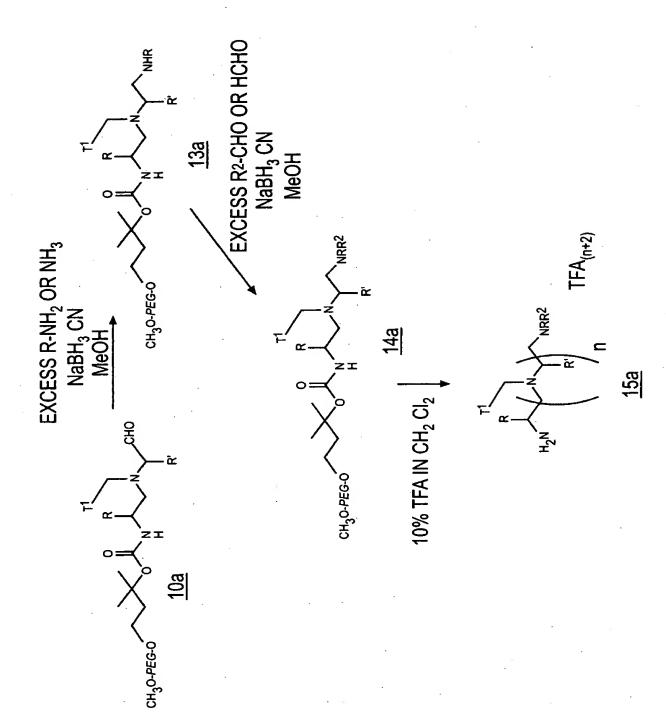
FIG. 34

FIG. 35





F/G. 36







$$H_3^{\bigoplus}$$
 H_4^{\bigoplus}
 $H_4^$

OTHER BASE/POLYAMINE LINKERS AS TERMINATORS

FIG. 38

FIG. 39

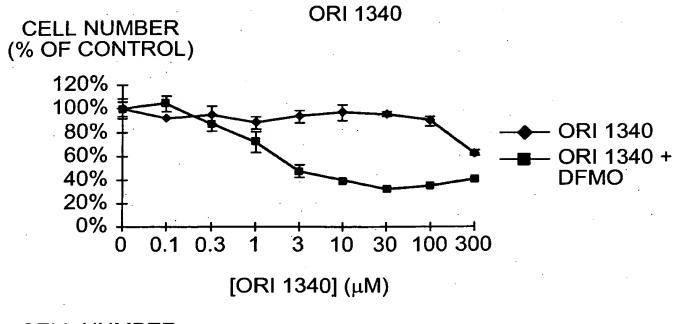


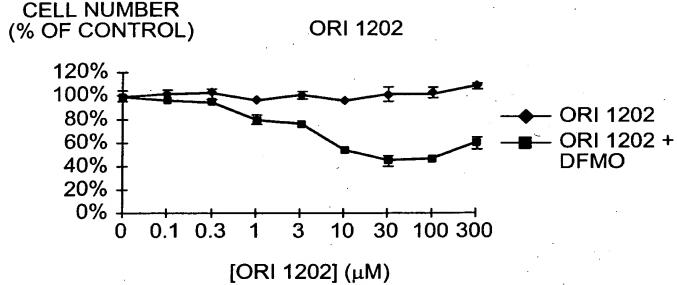
FIG. 40

FIG. 41

FIG. 42







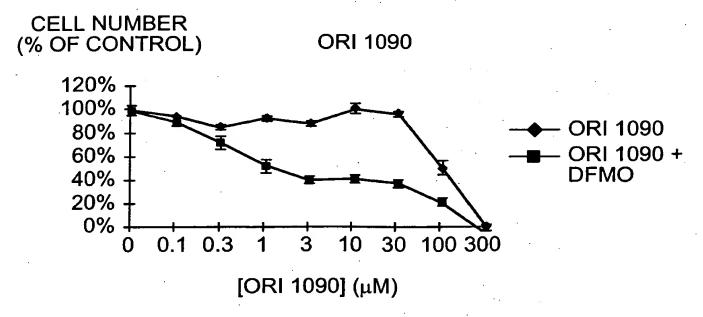


FIG. 43

ORI 1157 L-VAL-SPM PREFERRED NATURAL AND NON NATURAL AMINO ACID AMIDES OF SPERMINE.

FIG. 44a



n = 1 TO 12

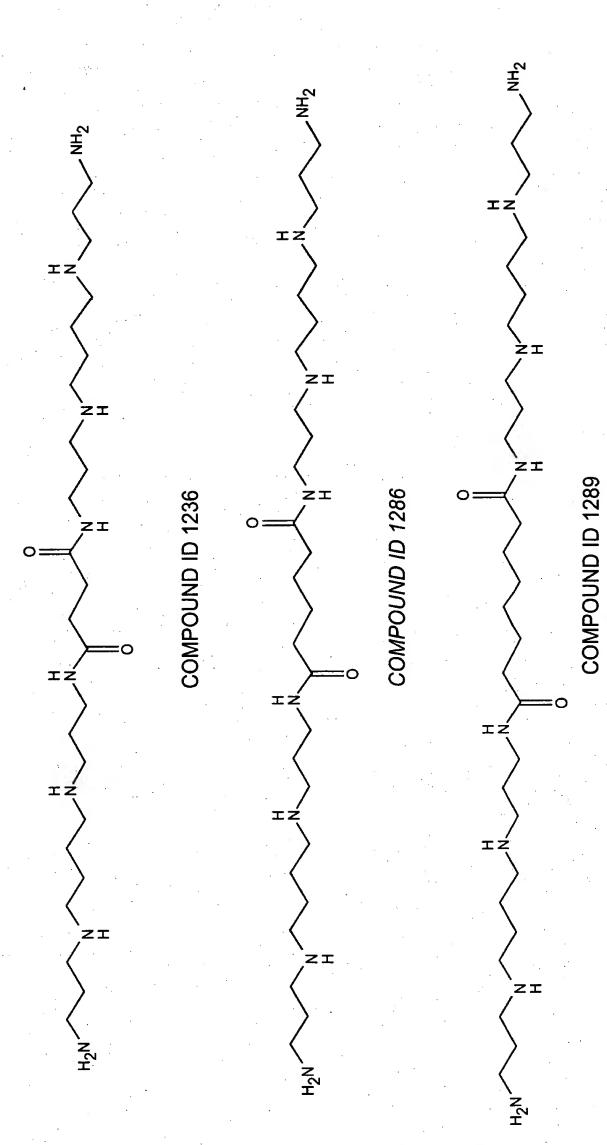
ORTHO, META AND PARA AROMATIC SUBSTITUTION

GENERAL STRUCTURE OF BIS-AMIDE DIMERS OF SPERMINE LINKED BY AN ALIPHATIC OR AROMATIC DI-ACID CHAIN.

FIG. 44b



REPLACEMENT SHEET



PREFERRED LINKED BIS-AMIDE DIMERS OF SPERMINE.

FIG. 44c



_											•	
	220	>300		×300	20	100	>300	œ	200		260	
	HALF EFFECT DRUG DFMO	3.58							22.3			
	GROWTH INHIBITION>CELL LINE	MDA		МБА	МДА	MDA	MDA	MDA	MDA		MDA	
	泾	0.19	0.083	1.0	0.28	0.084	>10	5	0.344* MDA	0.4	0.54	
	TRANSPORT>CELL LINE	MDA	MDA	MDA	MDA	MDA	MDA	MDA	MDA	MDA	MDA	mda
N1-MONOSUBSTITUTED POLYAMINES: AMIDES, NO LINKER	STRUCTURE				7 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		0 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 N - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	H H H H H H H H H H H H H H H H H H H		2-1 2-1 2-1 1-2	
MONOSUBSTITUTE	MOL WEIGHT	1032 387.5295		1033 421.9745	1035 516.5189	1037 472.6331	1038 407.9474	1039 502.4918	1043 407.5635			1072 595.8762
ž	. OI	_			_							

FIG. 45a



			MDA	>40			
1073	1073 306.4549		MDA	0.61	mda	150	>300
1076	426.9911	1, 2, 2, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1,	МДА	0.116	mda	28.1	150
			MDA	0.165*			
1077	1077 501.1143		MDA	0.11*	mda	2.46	98
			MDA	0.037			
1078	447.604		MDA	0.19*	mda		61
		H			g-od		19.4
					caco-2	-	24.4
					сеш		6.9
1079	1079 429.6323		MDA	0.594*	c-od		æ
					mda		78
1080	346.5202		MDA	0.062*	тда	7.4	190
			MDA	980'0			
1081	442.6531	1-10-7-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1	MDA	0.297*	mda		3 6
					pc-3		55
					caco-2		23.0
					шеэ		1.7
1104	457.4043	\$\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	MDA	0.12	mda		82
	-				pc-3		20.2
					caco-2		36.2
					cem		4.5

FIG. 45a (CONT. 1)

							•						
	>100	>100	>100	>100	>300	>300	·			·			
					0								
		H			>300	20.1	·						
	mda	H157	mda	h157	тда	pc-3							
83	ш	H	EL .	Ĭ,	0.0252 m	ď							
0.083					0.0								
MDA					MDA				,		·		¥.
1,0 N N N N N N N N N N N N N N N N N N N	1 N N N N N N N N N N N N N N N N N N N			Ι.			I, J, Z, N,					A WALL WALLOW	
1163 302.4638	230.36		256.3943		412.62		308.47	352.57	341.41	1213 328.4829	325.46	284.45	1216 313.49
1163	1166		1167		1169		1208	1210	1211	1213	1214	1215	1216

FIG. 45a (CONT. 2)



			>300	>300		·		
			>300	>300				
		1.14	mda	pc-3		~		
		МДА				MDA	MDA	
						± 5		
1217 307.44	1218 307.4424	1235 364.5792	1240 378.6062		1249 470.5594	1251 392.5053		1347 472.6795

FIG. 45a (CONT. 3)



7	2
5	
T	H
C	j

																					_	
	C50	, 6 6 7		٠.				× 6	450	380	72		25			79	>300	>100	6.9			150
	HALF FFFECT DRUG DEMO	2.2							0.63				\$	•		9.4	8.26					
	GROWTH INHIBITION>CELL LINE	MDA-MB-231 2.2 >100						MDA-MB-231	mda	mda	mcf-7	casmc	MDA			MDA	MDA	тда	mda			MDA
	Ξ	.024*	 0.16*	0.0339*	0.012	0.0152*	0.0078*	0.0245-0.13	0.0052-0.03	8.6nM			0.104		0.12		0.230					0.11*
·		MDA-MB-231	A172	PC-3									MDA		A172		MDA	·	MDA			MDA
NY MONIOSI IBETITI ITEO DOI VANINES: AMIDES MITU I INICED							-													-T.		
THETTOGING	MOL WEIGHT	1002 548.7972											99 472.6795			•	22 370.5425	401.5974	55 398.5718			1056 396.5807
		 8											1009				1022	1040	1055			ë i

				_				_		_	_	_	, 			<u> </u>	-
70	>300	360		560		85	× 6 7 8	>30	27	8.7	×30	29	8		% %		
	>300	\$		9.81			>100	>30					>30		>30		
mda	mda	mda		mda		mda	mda	mda	mda	pc-3	caco-2	cem			mda		
6.5	0.099	0.00895	0.0942	41.2 nM	57.8 nM	*88	>30	97.0	19.2*			,	*0.00	0.43	06^	×	D 74
MDA	мра	МБА	MDA	MDA	MDA	MDA	MDA	МДА	MDA			•	MDA	MDA	MDA	mda	MDA
	1					H.C. S. R. H. M.		5	P	H ₂ C ★ 3 B							
1059 546.822	1060 439.8164	1061 576.8513				1063 550.7666	1064 510.7013	1065 632.9597	1066 650.9722				1067 492.6888		1068 506.7567	1069 459.431	

FIG. 45b (CONT. 1)



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>100	>300		300							×300								190			1200	1200	>1000		
			0.960							1.54								26.5			5.24	5.52	263		
mda	тда		mda							mda								mda			mda	mda	mda		
	81.3	2.2	0.0147	0.00997	0.070*	0.01324	0.0252	0.013*	0.022*	13.3-15.7 nM	0.0216 Pre-	0.0273	0.0812	0.016	>30	19.2*	,		0.0397	0.117	0.0817		2.1		
	mda .	mda	mda	MDA	PC-3	MDA	MCF-7	CaCo	MDA	MDA	MDA	MDA	HT-29	Du145	mda			MDA	MDA	MDA	MDA		MDA		
				ا ا ا ا ا ا ا					3						<u>-</u>		#\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	"Anthony and the Month of the Market			Down hand	70		"Option to the company of the compan	
1083 401.5974	1085 373.5025	1086 481.6	1090 629.2897												1093 630.9845			1096 594.8446			1097 455.6678		1098 590.8348		

0.0164 0.0105* 0.010663 0.00663 0.00793 pc-3 0.19 0.19 0.0167 mda 0.073 pc-3 0.073 pc-3 0.073 pc-3 0.073 pc-3 0.0568* pc-3 0.0568* pc-3 0.0568* pc-3 0.0568* pc-3 1.44	Confirmite the MDA MDA MDA	MDA MDA		0.0195* 0.00485	mda	0.588	180
MDA 0.0105 MACF-7 0.0106 MACF-7 0.			PC-3	0.0164			
			MDA	0.0105*			
CaCo 0,00663 We will be seen a caco 0,00793 pc.3 We will be seen a caco 0,00793 pc.			MCF-7	0.0196			
### MDA 0.0793 pc-3 ###################################			CaCo	0.00663			
	7907	E-	MDA	0.0703	2	V	900
	767	~#~~;!~~	MUA	0.0733	pc-3		>300
### MDA 0.182 mda ###################################				,	mda		>300
	5186		MDA	0.182	тда		83
MDA	7189	ŎijĠ~~Ŷŗ~ĹĸĬ	MDA	0.19			-
「	.8402		MDA	0.0167	mda	1.44	380
		Ç. 0					
	0029		MDA	0.073	pc-3	1.43	320
「					mda	1.59	×300 ×300
Pc-3 mda mda pc-3 mda pc-3 mda pc-3 mda pc-3 mda pc-3 mda pc-3	7012						
					pc-3		×300 ×300 ×300
「					mda		×300 800 800 800 800 800 800 800 800 800
#cークサール MDA 0.0568* pc-3 mda mda mda mda mda mda mda mda	7012				pc-3		>300
#c-Colland MDA 0.0568* pc-3 mda mda mda mDA 0.0687* mda)))			mda	315	Š 8
mda "550 H	6949		MDA	0.0568*	pc-3	5.1	웃
HS. O. H. C. L. L. H. MDA		±		-	mda	11.5	<u>خ</u>
	6245	\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	MDA	0.0687*			

FIG. 45b (CONT. 3)

		255	530			>300			>300	×300	× 86 8		>100	>1000	>1000	×100	66	>400	×300 8	×300	>300	28	>300	×38
		5.20	1.23			13.2			68.2	71.3	29.2		66.5	9.68	9.23	>100			1.55	2.56	45.8		>300	>300
		MDA	PC-3			mda			mda	pc-3	pc-3		mda	mda	pc-3	mda	pc-3	mda	mda	pc-3	mda	pc-3	mda	pc-3
0.248	0.397	·	0.0136 F		0.0985	0.0178 n		0.0466			0.167* F	•		_	0.0344		0.0903	0.085	0.00955 r		0.0564*		>0.3	>1
MDA	MDA	MDA	MDA	PC-3	Du145	MDA		MDA	MDA		MDA			MDA	MDA	MDA	MDA	MDA	MDA	-	MDA		MDA	MDA
		" La	# #				# # # # # # # # # # # # # # # # # # #		".c. L. H. L.						0	#c-5-4				— >Œ	","—#~~#~~#~~# ","—#~~#~~#		"" "" "" "" "" "" "" "" "" "" "" "" ""	
1122 343.5604		1122 657.3438				1124 576.8513		_	1129 529.7915		1135 425.6633			1136 477.7398	_	1149 387.5703	1152 490.8377		1156 614.275		1160 393.5961	_	1161 357.5438	
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FIG. 45b (CONT. 4)

KEPLACEMENT SHEET

199	188	>300	×300	×300	>300	>300	>300	Š		277	77.	Š	>300	2300	>300	235	8	195	173
		>300		>300			>300	>300 -				,		7.					
mda <3	5>	mda >3	pc-3		pc-3	3 .	mda >3	pc-3		mda 62	pc-3		pc-3		pc-3		pc-3	mda	pc-3
0.0143 n	0	n	d	0.061 n	d	1>uM	0.0265 n	.		7			0.0185* p			7			
MDA		MDA		MDA		MDA	MDA			MDA		MDA	MDA	MDA		MDA			
Confirmation of the state of th		">~~\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\		"					M+CPE30 H H	H,C			> > =0					" Lykykyky	
1165 607.2209		1174 459.66		1175 373.5432		1179 369.555	1180 439.6684		1203 244.3832	1209 359.52		1233 587.2084		1234 506.7159		1238 364.5792		1239 392.6333	

FIG. 45b (CONT. 5)



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0.0262			0.46			0.0577	⋋							
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			2	·						*				
MDA			MDA	:		MDA	MDA				,			
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5.2626	428.6448		3.5189	313.4495		505.666	392.6333			413.5865	348.5361	7.4338	644.3043	
1241 615.2626	1243 428	_	1244 359.5189	1245 313		1254 505	1281 392	\dashv	-	1298 413	1305 348	1315 477.4338	1340 644	\dashv
12	12		17	12		12	12	-		12	55	13	ا ا	

FIG. 45b (CONT. 6)



	1050	× 100	>300	>1000		>300			T	>300	×300	\$		>100	>100	>300	Ş	108	>100		~300 200	460
	HAI E EEEFT NDI IC DEMO		18	515		54	*	·		>300					^	>300	8	0			•	>300
	GROWTH INHIRITIONS CELL I INF	mda	mda	mda		mda		MDA		MDA	PC-3			mda	mda	mda	00-3	MDA	PC-3		MDA	PC-3
	字	=	0.075	0.117	0.040	0.028-	0.043	0.162	0.190	0.64	0.5	0.248	0.397	>10	0.043*	0.0756* mda	0.0636			6	0.39	
	TRANSPORT>CFI 1 2 INF		MDA	MDA	MDA	MDA	MDA	MDA			MDA		MDA	MDA	MDA	MDA	PC-3	Du145		ACA	MDA	
	N1-MUNOSUBSTITUTED POLYAMINES: AMIDES, AMINO ALKYL D MOL WEIGHT STRUCTURE	x-x	I=I 					Z-I Z-I Z-I Z-I		T-2				Z-I	I = I = I = I = I = I = I = I = I = I =					I.	**************************************	
11.100	OSUBSTITUTE MOL WEIGHT	301.4791	315.5062					244.3832		343.5604		343.5604		301.4791	287.452	273.4249				204 4704	1874.100	
	NJ-MON- ID	1091	1094					1110		1121		1122		1126	1150	1177)BI -	

FIG. 45c



>300	>300
>300	299
МДА	PC-3
0.424	
MDA	
301.4791	
1198	

FIG. 45c (CONT.)



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	1050	>100	>300	>100		>100						
	HALF EFFECT DRUG DFMO		22.64	50.4		>100						
	GROWTH INHIBITION>CELL LINE	mda	c-od	mda		mda						
	泾	0.232*				.860.0	<u>~</u>	0.156	0.258	0.183	0.0913	0.083
MINO ACID HEAD GROUP	TRANSPORT>CELL LINE	MDA				MDA	MDA	epu.	MDA	MDA	MDA	MDA
N1-MONOSUBSTITUTED POLYAMINES: AMIDES, PROTECTED AMINO	STRUCTURE	45 Ho				1-x	1 0 Z - I - I - I - I - I - I - I - I - I -		100 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1			-±
OSUBSTITUTE	MOL WEIGHT	359.5161	488.679		458.6526	1147 481.7281	1151 416.5685	430.5955	1155 401.5974	399.5815	1162 433.6614	
N1-MON-IN		1117	1118		1127	1147	1151	1153	1155	1158	1162	

>300	>300	50	20	>300	>300	>300	>300	^300	×360	>300	×300	>300	>300	>300	>300
>300	>300	·		>300	14.0	>300	14.0	>300	14.0	>300	14.0	>300	14.0	25	100
mda	pc-3	mda	pc-3	nda	pc-3	epu	0-3	nda	ic-3	epu	ic-3	epu	pc-3	ADA	PC-3
<u> </u>	đ	37.1 n	d.	0.0418 mda	a	0.0418 mda	bc-3	0.0418 n	c-3d	0.0418 n	bc-3	0.0418 n		0.465 1	
MDA		MDA		MDA	MDA	MDA	MDA		MDA	MDA	MDA		MDA	MDA	
		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	·			1-x 1-x 2-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1				1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		1-1 1-1 2-1 3-1 1-1 1-1 1-1 1-1 1-1 1-1 1-1 1-1 1		H,C CH, H,C CH	70.00
1170 521.7061		1172 555.7673		1176 373.5432		1176 373.5432		1176 373.5432		1176 373.5432		1176 373.5432		1189 493.6956	

FIG. 45d (CONT.1)



REPLACEMENT SHEET

>300	>300	>300	>300	>300	>300	000	000 000 000 000 000 000 000 000 000 00	×360	>300	>300	430	>300	Š	>300
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>300	89.2	91.9	37.9	70.9	15.5	0 20	29.8	41.3	7.87	36.9	16.9	<u>\$</u>	Š	6
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pc-3		PC-3		PC-3	0.060* MD	IS IS	39 MDA	8	PC:3		pc-3	mda	pc-3	094 md
	0.265		0.271		<u>0</u>	-	0.039		+	0.191	H			0.1
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	,													
	MDA		MDA		MDA		MDA			MDA				MDA
	<u>*</u>		T-1		<u> </u>					Z-1		- X - I		
					}:					} } }		ž-±		* _ * _ * _ * _ * _ * _ * _ * _ * _ * _
	z-ź		z-ź		x-x		r-z			z-z		-		} ~~r
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		2		ľ							1		C	
_	5 (9		₹ , (5‡		H.C.X.		7. 7. 9.X	_	_	H,C OH,		£ X	_	T, T
	.6245		.59/4		<i>(1)</i> :		.6567			.6392	- 2002	/690	2770	5173
	1193 415.6245		1195 401.59/4	-	1199 564.775 		1200 464.6567	\dashv		1201 430.6392	20,	1205 403.5697	200	1200 383.3773
	~				-		-			—			-	-

FIG. 45d (CONT.2)



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	33	62.	96	121	245	245	117
	1219 387.5703	1221 550.7479	1222 450.6296	1223 416.6121	1229 415.6245	1231 415.6245	1259 760.9417
	1219	1221	1222	1223	1229	1231	1259
1				1			

FIG. 45d (CONT.3)



	020	0000			560	>1000	>300	>100		>300		>1000	>300	>300	>100		>300	>300	>300	>300	2300×	×38		
	HALF EFFECT DRUG DFMO	C.C			8.44	14.05	30.0			57.0		81.97	113	25			>300	>300	5.58	14.35	26.42	3.86	5.28	
	GROW I H INHIBITION>CELL LINE HALF EFFECT DRUG DFMO	8 0.		mda		pc-3	mda	mda		pc-3		mda	mda	pc-3	mda		mda	pc-3	mda	00-3		_	pc-3	
B) s	M 0 072	200	-			0.011-		0.07	0.1036*						0.214*		0.047		0.160*	0.0392	0.149	0.109	0.0514	0.0467
HA-AMINO ACID HEAD GRO	I KANSPOKI > CELL LINE					MDA		MDA	MDA	MDA					MDA		MDA		MDA	MDA	PC-3	Du145	MDA	Du145
N1-MONOSUBSTITUTED POLYAMINES: AMIDES, NATURAL ALPHA-AMINO ACID HEAD GROUP	S I KUC I UKE	_	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	-x =0				x - z / c - z / c - z / c / c / c / c / c / c / c / c / c /		T	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1				\bigcirc	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	I - Z T - Z					*		
MOSUBSTITUTE	1005 388 5607	200000			,			259.3978		316.4501	·				349.5237		1154 330.4772		301.4791					
N1-MON	ارة الق	2			. :			1125		1131					1148		1154		1157					

FIG. 45e

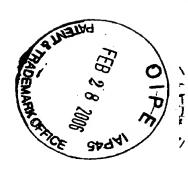


>300	>100	>100		>300	×300	>300	>300	>300	>300	>300	>300	>300	>300		>300	>300				
92.8	16.5 >100	12.1		>300	300	185	94.6	42.7	>300	>300	300	213	25.5	20.8	4.75	5.30	[17]			(CONI.2)
0.0255 mda	0.0499 pc-3 0.21.5-50 MDA			DC-3	0.0765 MDA		0.0768 MDA	PC-3	0.0526* mda	pc-3	0.167 MDA		0.0453 MDA	PC-3	0.0295 MDA	0.748 PC-3		0.03£	0.185	F/G. 45e (CC
MDA	MDA		СМ3		WDA	MDA	MDA MDA		MDA		MDA	MDA	MDA			H	MDA	MDA	HT-29	7.0
x-Z		**	Ì		I - 2 - 1 - 2		H_N_N_N_N_N_N_N_N_N_N_N_N_N_N_N_N_N_N_N		T		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		T Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z		T - 2 - 1 - 2 - 1 - 2 - 2 - 2 - 2 - 2 - 2					
1159 299.4632		1164 333 5431			1171 331.462		1173 365.5231		1178 273.4249		1186 317.4349		1187 289.4243		1202 330.5209					AND INC

THO PART CHARGE CAN STATE OF THE STATE OF TH

>300	>300	>300	>300	>300
6.5	62 9.1	>300	>300	>300 6.80
mda	pc-3 mda	pc-3 mda	pc-3 mda	pc-3 mda pc-3
0.13 m	0.124 m	0.0323 mda	0.113 E	g 660.0
МБА	MDA	MDA	MDA	MDA
T	Z-I Z-I Z-I Z-I Z-I	T = T		
1207 303.4514	1228 315.5062	315.5062	374.6181	1260 358.5343
1207	1228	1230	1237	1260

FIG. 45e (CONT.3)



1050	320	214	>300	000	300	× 88	>300	>300	>300	>300	>300	- 8	>300	>30	×30	
HALF EFFECT DRUG DFMO			5.32	7 54	16.19	1.82	9.03	8.01	8.0	2.4	3.0		4.37	7.8	0.95	
GROWTH INHIBITION>CELL LINE		PC-3	MDA	PC_3	MDA	Pc-3	MDA	PC-3	mda	pc-3	pc-3		mda	mda	pc-3	
30UP	>1 µM MDA	10.6 PC-3	0.0727*			P.53	0.0483		0.16		0.0432 pc-3		0.0515 mda	0.241		
LPHA-AMINO ACID HEAD C TRANSPORT>CELL LINE	MDA						MDA	-	MDA		MDA		MDA	MDA		
N1-MONOSUBSTITUTED POLYAMINES: AMIDES, NON-NATURAL ALPHA-AMINO ACID HEAD GROUP ID MOL WEIGHT STRUCTURE Ki	T = T		1,004 1,004 1,104				H-0 0 0 H-1		1, 0, 0, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1,		±	T. Z-I		1, 2 = 1		
SUBSTITUTED MOL WEIGHT	313.4466		1194 315.5062				301.4791		287.452		316.4938			355.5715		1309 388.5607
N1-MONC	1188		1194				1196		1220		1224	·		1227		1309

FIG. 45f



F/G. 45g

	1050	>300		244.8				>10000
	HALF EFFECT DRUG DFMO	85		15.0	4.2	,	1.7	
	GROWTH INHIBITION>CELL LINE	mda 85 >300		pc-3	ерш		pc-3	mda
	Ki							
RIVATIVE HEAD GROUP	TRANSPORT>CELL LINE	7	r					
N1-MONOSUBSTITUTED POLYAMINES: AMIDES, AMINO ACID DERIVATIVE HEAD GROUP	MOL WEIGHT STRUCTURE	418.6337	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		510.7726			145.206
N1-MONOSI	Q	1304			1310			1355



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	I) EO	009		>300	28 uM		40 uM	20			50	>300		>300	6	07	18
	HAI F FEFECT DRIIG DEMO	20		100uM				*) 11	1.05
	GROWTH INHIBITIONS CELL LINE	MDA 20	A172	MDA	A172		MDA	A172			MDA	mda		MDA	MDA		MDA
	ž	.039	90:		23			1.46		·		09		>10	0 110		0.082
	TRANSPORT>CELL LINE	MDA	A172	MDA	A172			mda				A172		MDA	MDA		A172
N1-MONOSI IRSTITI ITED DOI VAMINES: SI II FONAMINES		1.7 1.7		₹	= .			*\		~ z-=		00/	I, , , , , , , , , , , , , , , , , , ,	2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2	I-2		
RSTITI ITED P	MOL WEIGHT STRUCTURE			421.6094	318.3975		7070 077	440.0 104	0)0			302.4389		416.6308	442.6282		
N1-MONOS!	D	1001		1003	1005		0007	92				1007		1008	1010		

			·															
20		50	150		90	ų.		100		2	15	>30	18.2	>30	13		20	
		<30			13.4										-		14.2	
6.0	•	>			=												122	
	÷														- 0		-	
MDA	·	MDA	MDA		MDA			MDA			MDA	pc-3	caco-2	Cem	MDA		MDA	
.990'0			>10		3.5		1.34	>10			2.9	1.6	,		9		.187	.24
									-									
MDA	÷		MDA		MDA		4172	MDA			, MDA	A172			MDA		MDA	A172
	**************************************		- \	***		x-, f	1	Ξ.	()	r	7	7			-	ئر آ گرمن	\$	
						\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\			Z=I						~ ~ ~	} /* %		- T
£ 7			#)	£			چ پارلو		:	()() 9		-# .o
435.6365			421.6094		435.6365			421.6094			489.6881 H				475.661	<u> </u>	392.5676	
1011			1012		1013		Ш	1014	-	\perp	1015				9101		1017	
	•				<u> </u>													

FIG. 45h (CONT.1)

120	20	50	110	22			20	>300	50	>300	20
			<i>y</i> .		. 1				-		
											92
	7.5	4.4						·		<u> </u>	
	·										
·				-			·	,			
MDA	MDA	MDA	WDA -	MDA			MDA	MDA	MDA	MDA	MDA
											·
& &	0.2	23	₹ 	<u>8</u>		.075	5.4	4.3	2.7	2	11.4
mda	MDA	A172		MDA		A172	/IDA	MDA	МДА	MDA	MDA
=											
278.3758	392.5676	270 5284	9.920	466.6505			407.5823	365.501	364.5135	322.4322	421.6094
1018	1019	10201		1023			1024	1025	1026	1027	1028

FIG. 45h (CONT.2)

>300	>250	>300	20	50	>300	12	6.2	16.1	0.79	53.0	12.4	46.1	6.5	180	190			180	140	2
	125	<10	8	8.7		.95				12.6				£	<3.0			13	7.3	
MDA	MDA	MDA	MDA		MDA	МДА	pc-3	caco-2	cem			mda	pc-3	MDA	mda			MDA	mda	
3.4	0.08	0.43	0.24		0.84	0.066					i						0.13	0.228		0.32
MDA	MDA	MDA	MDA		MDA	MDA								MDA	NDA	MDA	ADA.	ADA	MDA	NDA
															2	2	~		M	2
379.5281	458.0054	393.5552	444.9505		430.5735	432.5893							007.07.	516.129				425.6192		
1029	1030	1031	1034		1036	1041							7.44	1044			,	1045		

FIG. 45h (CONT.3)

KEPLACEMENT SHEET

28	34.8	>30	8.9	170		>300	>300	140		>300		>300	20	20	10.8	27.1	2 k	100
·														è				
6.92				7.3		26.7		2.26		6.5		ಜ	<3.0	7 %0				
							,											
mda	pc-3	caco-2	Сеш	mda		mda	mda	MDA		mda		mda	MDA	mga	pc-3	caco-2	cem	mda
0.44	0.0677			0.375	0.177	0.421	2	0.108	0.0537	0.28	0.076	0.16*	0.025	0.0829				0.17
ΑC	Y(¥(MDA	AC	AC	A(A(K	¥.	A(Ą	A(A
WDA	MDA	-	·	WDW C	M	MDA	MDA	WDA	MDA			MDA	MDA	MDA		\dashv	-	MDA
													Ç,					
} }						zz	z-z	z-2		2=2 2=2		> ===≥	} ==={					$\frac{1}{2}$
				}	,	}	}_==			}			\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\					
472.6979				488.6944		400.5686	423.0024	494.0602		481.684		342.5071	445.8422					434.7334
1046				1047		1048	1049	1050	100	LCOL		1052	1054					105/

FIG. 45h (CONT.4)



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3.4
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9		5.9	14.8	0.71	3	13	>30	×30	Š			 140		88	4	160	150	>300
																		>300
mda		5-50	caco-2	cem		nda	pc-3	300-2	HA.	MDA		mda		3.5 and a	mda	mda	mda	~ mda
0.17*))	>10)	>30	>100	£<	5.4*	 0.067	0.083	0.094	0.19	0.22
MDA					MDA MDA	10.000				MDA	MDA	MDA	mda	MDA	MDA	MDA	MDA	MDA
													Ξ-				1 - 2 - 2 - 1 - 2 - 2 - 2 - 2 - 2 - 2 -	T-T OBMO
484.7503	¥ -			·	287.787				,	437.606	433.6206	412.6426	278.3758	488.6944	557.6804	356.5342	322.5167	294.4625
1058					1070					1074	1075	1082	1088	1103	1105	1106	1108	1130

FIG. 45h (CONT.6)

348.5329

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_	_	Τ.			_		·		
	<u>55</u>				5				
	HALF EFFECT DRUG DFMO			:					
	GROWTH INHIBITION>CELL LINE HALF EFFECT DRUG DFMO IC50				MDA				
	.Y				2.2	3			
AMINES	TRANSPORT>CELL LINE	*			MDA	A172		46	
N1-MONOSUBSTITUTED POLYAMINES: N1-MONOSUBSTITUTED AMINES	STRUCTURE			HC, N — H			≖− ₹		-I
BSTITUTED P	MOL WEIGHT STRUCTURE		372.4712				1350 316.5374		
N1-MONOSUI	₽		1004				1350		

FIG. 45i



REPLACEMENT SHEET

1050			8		~100	×100	
<u>121</u> 0M:	35		100		<u> </u>	\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	
HALF EFFECT DRUG DF	8.2		14.8		30	95	
H.							
GROWTH INHIBITION>CELL LINE HALF EFFECT DRUG DFMO	мра		MDA		pc-3	mda	
泛	0.44	.			0.0674 pc-3	0.090	%
TRANSPORT>CELL LINE	МДА	A172	MDA	MDA MDA	MDA	MDA	MDA
NI-MUNOSUBSTITUTED POLYAMINES: OTHER MOL WEIGHT							
MOSUBSITIUI MOL WEIGHT	421.5906		569.7752	641.0454	563.8118		591.735
N1-MO ID	1021 (UREA)		1042 (UREA)	1071	1109 (UREA)		1295 (THIOUREA)

FIG. 45j



								_				
1050	29	. •			>100	× 50 70	45.8		20.5			59.2
HALF EFFECT DRUG DFMO												15.0
GROWTH INHIBITION>CELL LINE				MDA	mda	h157	mda		pc-3			mda
Z	4	_	11.6*	8.44*			7.4			0.38	0.44	
TRANSPORT>CELL LINE	MDA		МDА	MDA			MDA		•	MDA	МДА	
N1, N12-DISUBSTITUTED POLYAMINES: N1,N12-DIACYLPOLYAMINE MOL WEIGHT STRUCTURE			140 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		\$\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\							
2-DISUBSTITUT MOL WEIGHT			628.9035		324.4702		554.867	·		1042.21	516.6923	582.9211
N1, N12 ID	1099		1132	1133	1168	-	1242			1250	1258	1282

FIG. 46a



120		198.0	42.83	>300	 මූ	156.7	83.6	195.5	6.09	195.2	199.5	64.1	24.9	6.4	6.4	185.5	183.5
1,		-	4	^	^		8	-	9	<u> </u>	=	9	2				-
													0				
3						·											
10.3																	
		·															
														·			
pc-3	,	mda	pc-3	mda	pc-3	mda	c-od	mda	pc-3	mda	pc-3	mda	bc-3	mda	pc-3	mda	bc-3
ă		<u> </u>	ď	Ε	ď		d	E	d	LI.	d	E	d	П	٥		<u>a</u>
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:	}	}_ <u>-</u>		\ 		<u>-</u>		}		<u>-</u>		}x		<u></u>	}	<u>-</u>	
										-}			ļ	070			
		ď		***		→		(_ ,, ⁵		- 		0.					
	275	6696		.981		792		1503		132		3948)135		159	
_	00 624.8275	1306 450.6699		31 594.7981		33 494.7267 		35 743.0503		36 740.7132		37 490.6948		38 743.0135		1339 590.8159	
	1300	13(1331		1333		1335		1336		1337		1338		13	

FIG. 46a(CONT)



GROWTH INHIBITION>CELL LINE | HALF EFFECT DRUG DFMO | IC50 0.104 TRANSPORT>CELL LINE MDA , N12-DISUBSTITUTED POLYAMINES: N1,N12-ACYLSULFONYLPOLYAMINES | MOL WEIGHT | STRUCTURE MOL WEIGHT 1266 763.4255 1276 522.7589 1280 687.3267

FIG. 46b



KEPLACEMENT SHEET

_		 			γ	· · · · · ·			т —
	<u>5</u>	0.74	0 61	1.27	0.84	21.3	33.2	2.0	1.9
	HALF EFFECT DRUG DFMO								
	GROWTH INHIBITION>CELL LINE HALF EFFECT DRUG DFMO IC50	mda	pc-3	mda	pc-3	mda	pc-3	mda	pc-3
	Ķi								
-	TRANSPORT>CELL LINE								
N1, N12-DISUBSTITUTED POLYAMINES: N1,N12-DIALKYLAMINEPOLYAMINES	STRUCTURE	" Chiling The							
-DISUBSTITUT	MOL WEIGHT	1247 534.53				520.5061		717.0217	
N1, N12	l al	1247		÷		1279		1352	

FIG. 46c



REPLACEMENT SHEET

GROWTH INHIBITION>CELL LINE | HALF EFFECT DRUG DFMO | 1C50 161 mda ဗ္ဗ 11, N12-DISUBSTITUTED POLYAMINES: N1,N12-ACYLALKYLAMINEPOLYAMINE | MOL WEIGHT | STRUCTURE | TRANSPORT>CELL LINE | 1270 | 544.7001 | 1

FIG. 46d



KEPLACEMENT SHEET

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1550		2.0	1.9	2.03	1.81	89	.51	55.9	25.6	9.4	5.2	>300	147			
HALF EFFECT DRUG DFMO K	├			[2		0	0	\$	2	6		*				
GROWTH INHIBITION>CELL LINE		тда	pc-3	mda	c-od	mda	pc-3	тда	bc-3	mda	6-3	mda	pc-3			
ïZ	0.19			-												
YAMINE TRANSPORT>CELL LINE	MDA															
N12-DISUBSTITUTED POLYAMINES: N1 N12-DISULFONYLPOLYAMINE MOL WEIGHT STRUCTURE	Ş							HCO-18-18-18-18-18-18-18-18-18-18-18-18-18-		acinimini in					0=0=0 1=2 1=2 2=1 0=0=0	
ISUBSTITUTED MOL WEIGHT	1278 829.91	662.8332						510.7229		648.8929		598.7916		775.0434	1329 494.7202	
N1, N12-D	1278	1293						1321		1322		1323		1328	1329	

KEPLACEMENT SHEET

	1050	
	HALF EFFECT DRUG DFM(·
	GROWTH INHIBITION>CELL LINE HALF EFFECT DRUG DFMO IC50	
	Ķį	
AMINEPOLYAMINE	TRANSPORT>CELL LINE	
2-DISUBSTITUTED POLYAMINES: N1, N12-SULFONYLALKYLAMI	STRUCTURE	
DISUBSTITUTED PO	MOL WEIGHT	1349 598.6832
N1, N12-	⊆	132



FIG. 46f





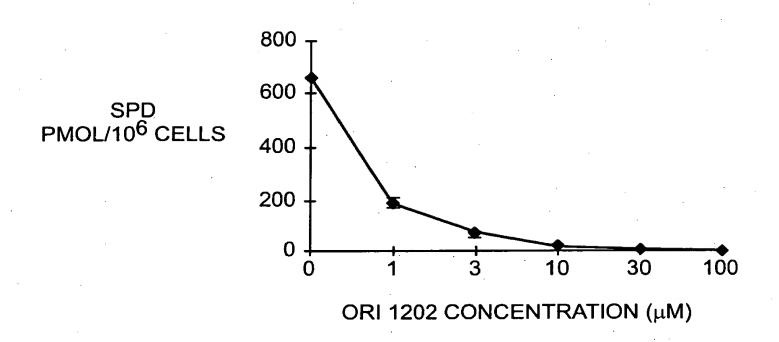


FIG. 48



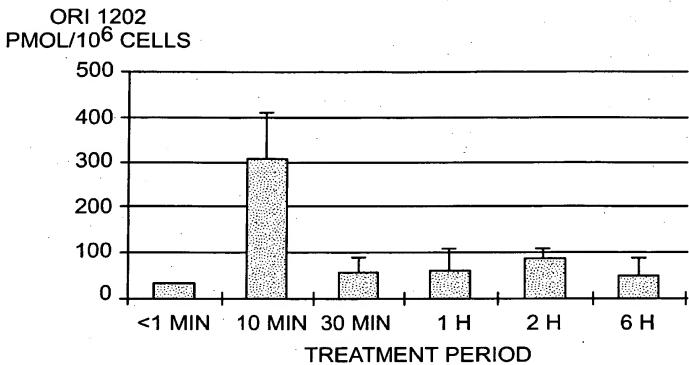


FIG. 49A

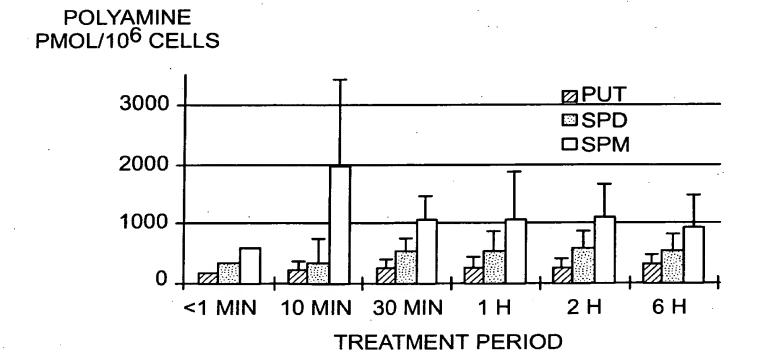
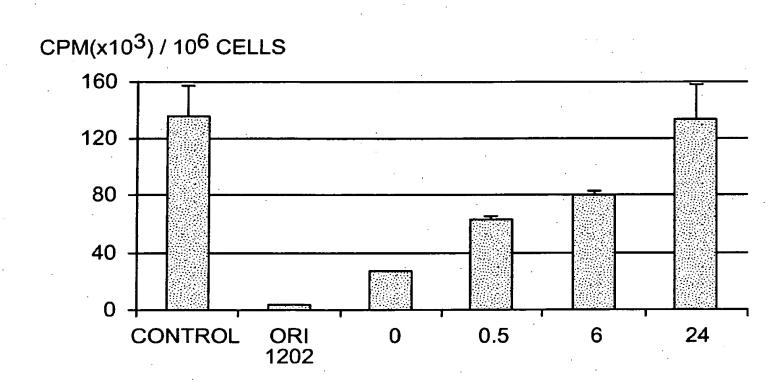


FIG. 49B





RECOVERY TIME (HOURS)

FIG. 50



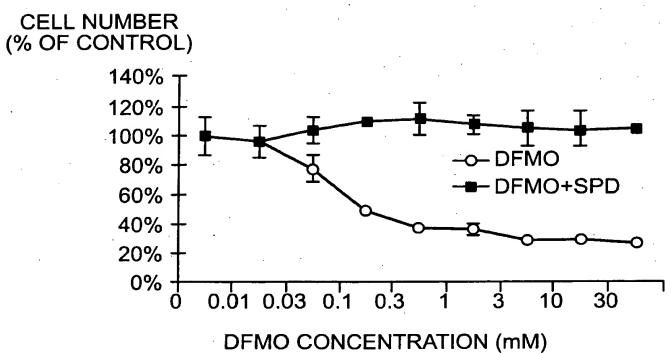


FIG. 51

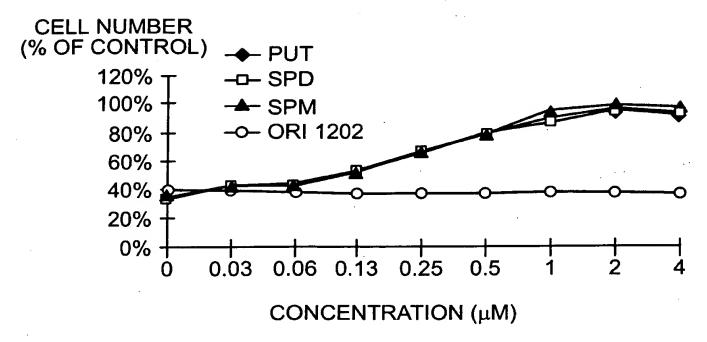


FIG. 52





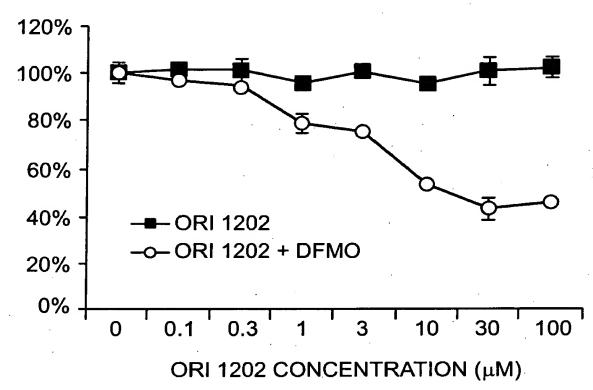


FIG. 53



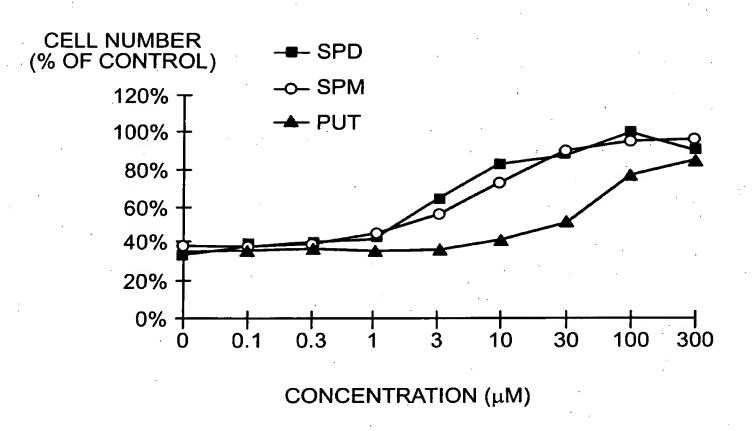
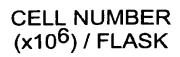


FIG. 54





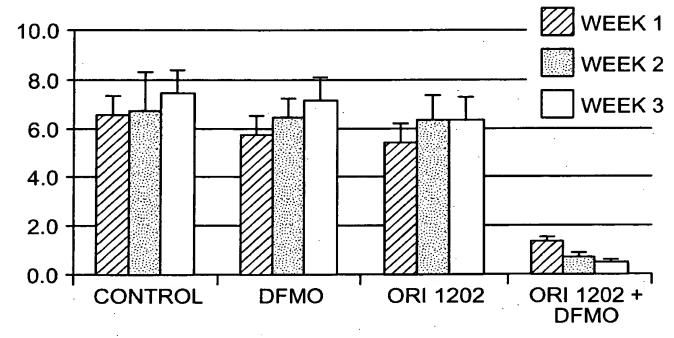


FIG. 55



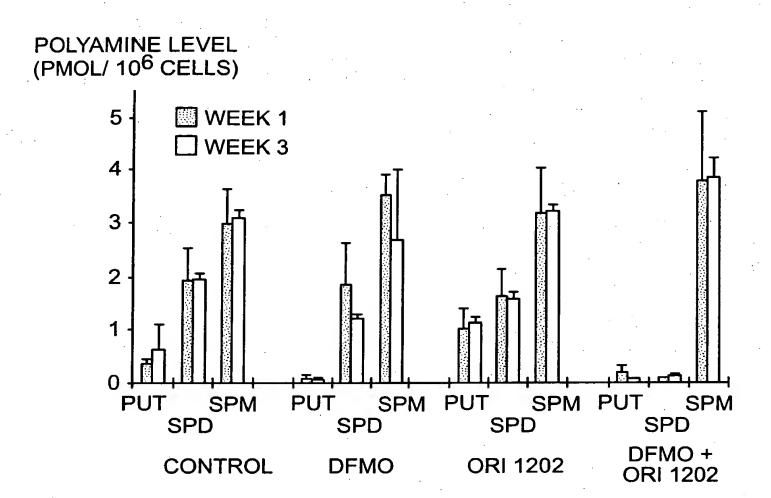
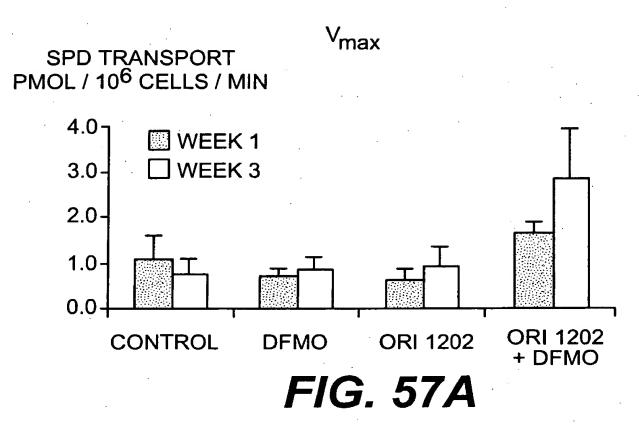
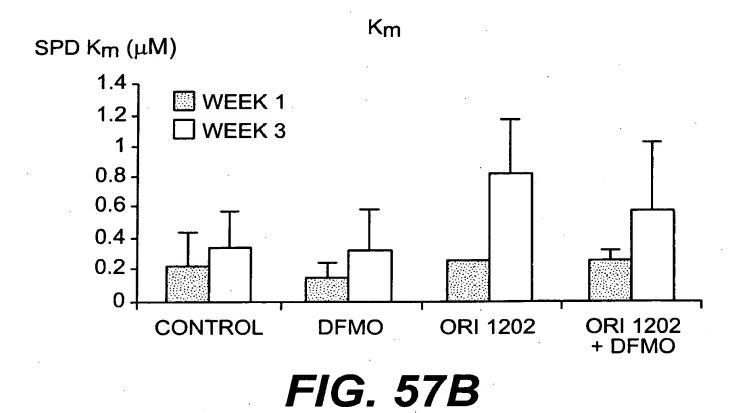


FIG. 56







POLYAMINE LEVELS (pmol/MILLION CELLS) IN MDA CELLS AFTER EXPOSURE TO ORI 1202 (30 M)

		×	(X)	(XS	9X)
	6 HR.	48.5 (1.5X)	935.8 (1.5X)	519.5 (1.5X)	318.5 (1.8X)
	O ,	48.	935	519	318
	2 HR.	85.3	1095.4	591.8	291.6
•	⊘ I		-	(D)	(7
	1 HR.	40.2	1071.17	554.6	279.7
				$\overline{}$	
	Z	(1.6X	(1.7)	(1.5X	(1.5)
	30 MIN.	52.2 (1.6X)	1038.2 (1.7X)	529.2 (1.5X)	269.2 (1.5X)
	z	(6.1X)	(3.2X)	(1.0X)	(1.2X)
·	10 MIN	198.5 (1955.2	358.3 (217.9 (
_	•	19	195	35	21
BACKGROUND	zi	<u>×</u>	X	X	X
GR (32.5 (1X)	606.8 (1X)	345.2 (1X)	180.2 (1X)
BACI	VI	35	09	34	18
			7.	9.	
•			591.7	398.6	217.5
		202			-
,		ORI 1202	SPM	SPD	PUT

FIG. 58



KEPLACEMENT SHEET